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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Oren Becker

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THE NATH LAW GROUP

112 South West Street

Alexandria, VA 22314

EXAMINER

LIN, JERRY

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/718,425	<b>Applicant(s)</b> BECKER ET AL.	
	<b>Examiner</b> JERRY LIN	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) 18-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 and 22-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Applicants' arguments, filed October 30, 2008, have been fully considered and they are deemed to be persuasive in-part. In light of recent court decisions, a new rejection is applied. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

#### ***Status of the Claims***

Claims 1-17 and 22-25 are under examination.

Claims 18-21 are withdrawn.

#### ***Claim Rejections - 35 USC § 101***

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-17 and 22-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Instant claims 1-17, 24 and 25 are drawn to a method of predicting an amino acid sequence that folds into a specified 3D structure. However, as the method does not recite a physical transformation of matter, the method must be tied to a machine to be patentable subject matter (For further explanation see, *In Re Bilski* (No. 2007-10030, decided 10/30/2008)). In the instant case, the claimed method steps are not tied to a machine, and thus are non-statutory.

Art Unit: 1631

Instant claims 1-17 and 22-25 are drawn to a process involving the judicial exception of a computational algorithm. Claims drawn to a judicial exception is non-statutory unless the claims include a practical application of that judicial exception as evidenced by a physical transformation of matter, or if the claimed invention recites a useful, tangible and concrete final result. In the instant claims, there is no physical transformation by the claimed invention, thus the Examiner must determine if the instant claims produce a useful, tangible, and concrete final result. See MPEP 2106.

The instant claims do not require a tangible final result. A tangible final result requires that the claim must set forth a practical application of the mathematical algorithm to produce a real-world result. The instant claims end with a step of outputting a computer output. However, a outputting does not necessarily mean that the output is communicated to the outside world. For example, the computer output could be in the form of a carrier wave. A carrier wave is not a tangible final result. Thus, the instant claims do not require a tangible final result. Examples of amendments to overcome this rejection include amending the claims to identify/recite a concrete result and to recite that the result is outputted to a display or to a user or outputted in a user readable format. However, applicant is reminded that any amendment must be fully supported and enabled by the originally filed disclosure.

#### Response to Arguments

4. Applicants have amended the instant claims to recite outputting a computer output. However as stated above, outputting may also encompasses carrier waves or outputting to another computer without communication to the outside world. Thus, the

Art Unit: 1631

instant claims do not have a practical application as evidenced by a useful, tangible, and concrete result.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-5, 9-17, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahiyat et al. (Protein Science (1996) Volume 5, pages 895-903) in view of Herzyk et al. (Proteins) Volume 17, pages 310-324).

The instant claims are drawn to a method of predicting an amino acid sequence by providing a coordinate set representing the backbone of a 3D structure, constructing a reduced virtual representation for the 3D structure, determining the amino acid

Art Unit: 1631

positions along the 3D structure, constructing an initial amino acid sequence, randomly selecting one or more positions along the sequence and applying a Monte-Carlo simulation, and expanding the reduced representation.

Regarding claims 1-5, 9-17, 22 and 23, Dahiyat et al. teaches protein design automation. Specifically they teach “We have conceived and implemented a cyclical protein design strategy that couples theory, computation, and experimental testing. The combinatorially large number of possible sequences and the incomplete understanding of the factors that control protein structure are the primary obstacles in protein design. Our protein design automation algorithm objectively predicts protein sequences likely to achieve a desired fold. Using a rotamer description of the side chains, we implanted a fast discrete search algorithm base on the Dead End Elimination Theorem to rapidly find the globally optimal sequence in its optimal geometry from the vast number of possible solutions. Rotamer sequences were scored for steric complementarity using a van der Waals potential. A Monte Carlo search was then executed, starting at the optimal sequence in order to find other high-scoring sequences. As a test of the design methodology, a high scoring sequences were found for the buried hybophobic residues of a homodimeric coiled coil base on GCN4-p1. The corresponding peptides were synthesized and characterized by DC spectroscopy and size exclusion chromatography. . . . A quantitative structure activity relation analysis was performed on the designed peptides, and a significant correlation was found with surface area burial. Incorporation of the buried surface area potential in the scoring of sequences greatly improved the correlation between predicted and measured stabilities and demonstrated experimental

Art Unit: 1631

feedback in a complete design cycle.” (Abstract). Specifically, Dahiyat also teaches that the PDA side-chain selection algorithm requires as input a backbone structure defining the desired fold. Also taught is that “using a rotamer description of side chains, an optimal sequence for a backbone can be found by screening all possible sequences of rotamers, where each backbone position can be occupied by each amino acid and all its possible rotameric states.” (page 896). (This corresponds to steps (a) through (d) of claim 1.) Also taught is “following DEE optimization, a rank-ordered list of sequences is generated by a Monte Carlo search in the neighborhood of the DEE solution. . . random position are changed to other rotamers, and the new energy is calculated. If the new sequence energy meets the Boltzmann criteria for acceptance, it is used as the starting point for another jump. . . after a predetermined number of jumps, the best scoring sequences are output as a rank-ordered list.” (Page 897). (This corresponds to step (e) of claim 1.) Also taught is that simpler structure measure, such as buried atoms, were used to resolve the structure of the amino acid. (page 899). (This corresponds to step (f) of claim 1.) Dahiyat et al. also teach using hydrophobic and hydrophilic positions to determine the structure (page 897). In regards to claims 10 and 11, since all positions are selected from the entire group of amino acids, Dahiyat et al. discloses the limitations of these claims. In regard to claim 23, Dahiyat et al. teaches using a computational method that would require use of a computer with an input apparatus, multiple memories, and a processor (page 901, right column).

However, Dahiyat et al. does not teach representing a protein wherein each amino acid has a backbone portion and side chain portion, where the backbone portion

Art Unit: 1631

is represented by a single sphere and the side chain of each amino acid is represented by one to two additional spheres.

Regarding claim 1, Herzyk et al. teach representing (i.e. a computer output) a protein wherein each amino acid has a backbone portion and side chain portion, where the backbone portion is represented by a single sphere and the side chain of each amino acid is represented by one to two additional spheres. (Abstract; page 312 and throughout. See also specification at page 9, lines 3-12).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Dahiyat et al. and Herzyk et al. One of ordinary skill in the art could have taken the data of Dahiyat et al. and represented that data in the teachings of Herzyk et al. One of ordinary skill in the art could have combined the elements as claimed by known methods with no change in their respective functions. Furthermore, the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

#### Response to Arguments

7. Applicants have responded by stating that the TSM test has not been discarded completely. The Examiner agrees that the TSM test has not been discarded; however it is only one test among many that may be used to show obviousness. In other words, the TSM test is not required to show obviousness. In the instant case, the claimed invention is obvious because elements as taught by the references are not changed and the combination would yield a predictable result. The invention is obvious not merely



Art Unit: 1631

because it could have been modified, but because the combination yields a predictable result to one of ordinary skill in the art.

Applicants also state that the references do not teach where there is a change in low resolution to high resolution as recited in part (f) of claim 1. However, part (f) of claim 1 has no recitation of resolutions. Thus, this limitation cannot be used to distinguish the claimed invention from the prior art.

Applicants also state that their method does not use the dead-end elimination algorithm. However, this limitation is not in the claims and cannot be used to distinguish it from the prior art. Read broadly, the instant claims may include the dead-end elimination algorithm.

Applicants also state that the method by Dahiyat et al. would yield only a low resolution structure. However, as stated before, the instant claims do not recite any limitations regarding the resolution of the claimed invention. Read broadly, the combination of Dahiyat et al. and Herzyk et al. teaches the limitations of the instant claims.

8. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahiyat et al. (Protein Science (1996) Volume 5, pages 895-903) in view of Herzyk et al. (Proteins) Volume 17, pages 310-324) as applied to claims 1-5, 9-17, 22 and 23 above, and further in view of Hurley et al. (JMB Vol. 224, 1992, pages 1143-1159).

Dahiyat et al. and Herzyk et al. are applied as above.

Art Unit: 1631

However, neither Dahiyat et al. nor Herzyk et al. teaches that the solvent is substantially water.

Regarding claims 6-8, Hurley et al. teaches design and structural analysis of alternative hydrophobic core packing arrangements in bacteriophage T4 lysozyme. Particularly, they teach, "in order to calculate stability changes in aqueous solution, the changes in free energies of transfer of the folded and unfolded states between water and vacuum must be obtained." (Page 1146).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teaching of Dahiyat et al., Herzyk et al., and those of Hurley et al. As Hurley et al. teach, it would have been obvious to determine the structure of an amino acid in water because it would have allowed for the calculation of stability change. Also, water would have been a common solvent for the amino acid structures to be found in nature, and therefore would have been obvious to use as it would have allowed for the closest approximation to nature. Furthermore, water would have been obvious solvent due to its neutral pH, low cost, and easy availability.

#### Response to Arguments

9. Applicants have responded to his rejection by relying on their response to Dahiyat et al. and Herzyk et al. Please see above for the examiner's response.

#### ***Withdrawn Rejections***

Art Unit: 1631

10. Applicant's arguments and amendments, filed October 30, 2008, with respect to the rejections made under 35 U.S.C. §112 1<sup>st</sup> and 2<sup>nd</sup> Paragraph have been fully considered and are persuasive. These rejections have been withdrawn.

### ***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JERRY LIN whose telephone number is (571)272-2561. The examiner can normally be reached on 7:00-5:30pm, M-TH.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 09/718,425

Page 11

Art Unit: 1631

/Jerry Lin/

Examiner, Art Unit 1631

1/20/09